CLAIMS

1. A polypeptide, which polypeptide:

   (i) comprises the amino acid sequence as recited in SEQ ID NO: 6;

   (ii) is a fragment thereof which functions as a nuclear receptor, or having an antigenic determinant in common with the polypeptide of (i); or

   (iii) is a functional equivalent of (i) or (ii).

2. A polypeptide according to claim 1 which:

   (i) consists of the amino acid sequence as recited in SEQ ID NO: 6;

   (ii) is a fragment thereof which functions as a nuclear receptor, or having an antigenic determinant in common with the polypeptide of (i); or

   (iii) is a functional equivalent of (i) or (ii).

3. A polypeptide which is a fragment according to claim 1(ii) or claim 2(ii), which includes the Nuclear Hormone Receptor Ligand Binding Domain region of the LBDG11 polypeptide, said Nuclear Hormone Receptor Ligand Binding Domain region being defined as including between residues 118 and 319 inclusive of the amino acid sequence recited in SEQ ID NO:6 and possesses activity as a Nuclear Hormone Receptor Ligand Binding Domain.

4. A polypeptide which is a functional equivalent according to claim 1(iii) or claim 2(iii), is homologous to the amino acid sequence as recited in SEQ ID NO:6, and has activity as a Nuclear Hormone Receptor Ligand Binding Domain.

5. A polypeptide according to claim 4, wherein said functional equivalent is homologous to the Nuclear Hormone Receptor Ligand Binding Domain region of the LBDG11 polypeptide.

6. A fragment or functional equivalent according to any one of claims 1-5, which has greater than 80% sequence identity, preferably greater than 85%, 90%, 95%, 98% or 99% sequence identity, with an amino acid sequence as recited in SEQ ID NO:6, or with a fragment thereof that possesses Nuclear Hormone Receptor Ligand Binding Domain activity, said sequence identity being determined using BLAST version 2.1.3

using the default parameters specified by the NCBI (the National Center for Biotechnology Information; http://www.ncbi.nlm.nih.gov/) [Blosum 62 matrix; gap open penalty=11 and gap extension penalty=1].

7. A functional equivalent according to any one of claims 1-6, which exhibits significant structural homology with a polypeptide having the amino acid sequence given in SEQ ID NO:6, or with a fragment thereof that possesses activity as a Nuclear Hormone Receptor Ligand Binding Domain.

8. A fragment as recited in claim 1, 2, or 6 having an antigenic determinant in common with the polypeptide of claim 1(i) or claim 2(i) which consists of 7 or more (for example, 8, 10, 12, 14, 16, 18, 20 or more) amino acid residues from the sequence of SEQ ID NO:6.

9. A polypeptide or polypeptide fragment according to any one of the preceding claims that is in the form of a dimer complex.

10. A dimer complex according to claim 9, which is a homodimer.

11. A dimer complex according to claim 9, which is a heterodimer.

12. A dimer complex according to claim 11, wherein said polypeptide or fragment is complexed with a polypeptide comprising a Nuclear Hormone Receptor Ligand Binding Domain.

13. A dimer complex according to claim 12, wherein the LBDG11 polypeptide or fragment thereof is complexed with the estrogen receptor α ligand binding domain, or the estrogen receptor β ligand binding domain.

14. A purified nucleic acid molecule which encodes a polypeptide or dimer complex according to any one of the preceding claims.

15. A purified nucleic acid molecule according to claim 14, which has the nucleic acid sequence as recited in SEQ ID NO:5 or is a redundant equivalent or fragment thereof.

16. A fragment of a purified nucleic acid molecule according to claim 14 or claim 15, which comprises between nucleotides 352 and 957 of SEQ ID NO:5, or is a redundant equivalent thereof.

17. A purified nucleic acid molecule which hybridizes under high stringency conditions with a nucleic acid molecule according to any one of claims 14-16.

18. A vector comprising a nucleic acid molecule as recited in any one of claims 14-17.

19. A host cell transformed with a vector according to claim 18.

20. A ligand which binds specifically to, and which inhibits or activates the Nuclear Hormone Receptor Ligand Binding Domain activity of, a polypeptide according to any one of claims 1-9 or a dimer according to any one of claims 10-13.

21. A ligand according to claim 20, which is an antibody.

22. A compound that either increases or decreases the level of expression or activity of a polypeptide according to any one of claims 1-9.

23. A compound according to claim 22 that binds to a polypeptide according to any one of claims 1-9 without inducing any of the biological effects of the polypeptide.

24. A compound according to claim 22 or claim 23, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.

25. A polypeptide according to any one of claims 1-9, a nucleic acid molecule according to any one of claims 14-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to claim 20 or claim 21, or a compound according to any one of claims 22-24, for use in therapy or diagnosis of disease.

26. A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claims 1-9, or assessing the activity of a polypeptide according to any one of claims 1-9, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.

27. A method according to claim 26 that is carried out *in vitro*.

28. A method according to claim 26 or claim 27, which comprises the steps of: (a) contacting a ligand according to claim 20 or claim 21 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and (b) detecting said complex.

29. A method according to claim 26 or claim 27, comprising the steps of:

a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 14-17 and the probe;

b) contacting a control sample with said probe under the same conditions used in step a); and

c) detecting the presence of hybrid complexes in said samples;

wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease.

30. A method according to claim 26 or claim 27, comprising:

a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 14-17 and the primer;

b) contacting a control sample with said primer under the same conditions used in step a); and

c) amplifying the sampled nucleic acid; and

d) detecting the level of amplified nucleic acid from both patient and control samples;

wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

31. A method according to claim 26 or claim 27 comprising:

a) obtaining a tissue sample from a patient being tested for disease;

b) isolating a nucleic acid molecule according to any one of claims 14-17 from said tissue sample; and

c) diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease.

32. The method of 30, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

33. The method of either claim 31 or 32, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridised portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and

detecting the presence or absence of an unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

34. A method according to any one of claims 26-33, wherein said disease is a disease in which Nuclear Hormone Receptor Ligand Binding Domains are implicated, such as cell proliferative disorders, including neoplasm, melanoma, lung, colorectal, breast, uterus, prostate, cervical, pancreas, head and neck and other solid tumours, myeloproliferative disorders, such as leukemia, non-Hodgkin lymphoma, leukopenia, thrombocytopenia, angiogenesis disorder, Kaposis' sarcoma, autoimmune/inflammatory disorders, including allergy, inflammatory bowel disease, arthritis, psoriasis and respiratory tract inflammation, asthma, and organ transplant rejection, cardiovascular disorders, including hypertension, hypotension, oedema, angina, atherosclerosis, thrombosis, sepsis, shock, reperfusion injury, heart arrhythmia, and ischemia, neurological disorders including, central nervous system disease, Alzheimer's disease, Parkinson's disease, brain injury, stroke, amyotrophic lateral sclerosis, anxiety, depression, and pain, cognition enhancement, learning and memory enhancement, developmental disorders, metabolic disorders including diabetes mellitus, osteoporosis, lipid metabolism disorder, hyperthyroidism, hyperparathyroidism, thyroid hormone resistance syndrome, hypercalcemia, hypocalcaemia, hypercholestrolemia, hyperlipidemia, and obesity, renal disorders, including glomerulonephritis, renovascular hypertension, blood disorders including hemophilia, dermatological disorders, including, cellulite, acne, eczema, psoriasis and wound healing, scarring, negative effects of aging, fertility enhancement,

contraception, pregnancy termination, progesterone antagonism, hormone replacement therapies, steroid hormone-like mediated hair characteristics, immunomodulation, AIDS, vision disorders, glucocorticoid resistance, mineralocorticoid resistance, androgen resistance, pseudohypoaldosteronism, spinal/bulbar muscular atrophy, extraskeletal myxoid chrondrosarcomas, adrenal insufficiency, sexual reversal, infections including viral infection, bacterial infection, fungal infection and parasitic infection, cancer, particular cancers originating from estrogen-responsive tissues, including breast, uterus, cervix and prostate, myeloproliferative disorders, such as leukemia, hypertension, hypotension, fertility enhancement, contraception, pregnancy termination, progesterone antagonism, wound healing, scarring, obesity, dermatological disorders including cellulite, estrogen-mediated hair characteristics, central nervous system disorders, Alzheimer's disease, cognition enhancement, learning and memory enhancement, immunomodulation and osteoporosis.

35. Use of a polypeptide according to any one of claims 1-9 as a Nuclear Hormone Receptor Ligand Binding Domain.

36. Use of a nucleic acid molecule according to any one of claims 14-17 to express a protein that possesses Nuclear Hormone Receptor Ligand Binding Domain activity.

37. A pharmaceutical composition comprising a polypeptide according to any one of claims 1-9, a nucleic acid molecule according to any one of claims 14-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to claim 20 or claim 21, or a compound according to any one of claims 22-24.

38. A vaccine composition comprising a polypeptide according to any one of claims 1-9 or a nucleic acid molecule according to any one of claims 14-17.

39. A polypeptide according to any one of claims 1-9, a nucleic acid molecule according to any one of claims 14-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to claim 20 or claim 21, a compound according to any one of claims 22-24, or a pharmaceutical composition according to claim 31 for use in the manufacture of a medicament for the treatment of a disease in which Nuclear Hormone Receptor Ligand Binding Domains are implicated, such as cell proliferative

disorders, including neoplasm, melanoma, lung, colorectal, breast, uterus, cervical, prostate, pancreas, head and neck and other solid tumours, myeloproliferative disorders, such as leukemia, non-Hodgkin lymphoma, leukopenia, thrombocytopenia, angiogenesis disorder, Kaposis' sarcoma, autoimmune/inflammatory disorders, including allergy, inflammatory bowel disease, arthritis, psoriasis and respiratory tract inflammation, asthma, and organ transplant rejection, cardiovascular disorders, including hypertension, hypotension, oedema, angina, atherosclerosis, thrombosis, sepsis, shock, reperfusion injury, heart arrhythmia, and ischemia, neurological disorders including, central nervous system disease, Alzheimer's disease, Parkinson's disease, brain injury, stroke, amyotrophic lateral sclerosis, anxiety, depression, and pain, cognition enhancement, learning and memory enhancement, developmental disorders, metabolic disorders including diabetes mellitus, osteoporosis, lipid metabolism disorder, hyperthyroidism, hyperparathyroidism, thyroid hormone resistance syndrome, hypercalcemia, hypocalcaemia, hypercholestrolemia, hyperlipidemia, and obesity, renal disorders, including glomerulonephritis, renovascular hypertension, blood disorders including hemophilia, dermatological disorders, including, cellulite, acne, eczema, psoriasis and wound healing, scarring, negative effects of aging, fertility enhancement, contraception, pregnancy termination, progesterone antagonism, hormone replacement therapies, steroid hormone-like mediated hair characteristics, immunomodulation, AIDS, vision disorders, glucocorticoid resistance, mineralocorticoid resistance, androgen resistance, pseudohypoaldosteronism, spinal/bulbar muscular atrophy, extraskeletal myxoid chrondrosarcomas, adrenal insufficiency, sexual reversal, infections including viral infection, bacterial infection, fungal infection and parasitic infection, cancer, particular cancers originating from estrogen-responsive tissues, including breast, uterus, cervix and prostate, myeloproliferative disorders, such as leukemia, hypertension, hypotension, fertility enhancement, contraception, pregnancy termination, progesterone antagonism, wound healing, scarring, obesity, dermatological disorders including cellulite, estrogen-mediated hair characteristics, central nervous system disorders, Alzheimer's disease, cognition enhancement, learning and memory enhancement, immunomodulation and osteoporosa.

40. A method of treating a disease in a patient, comprising administering to the patient a polypeptide according to any one of claims 1-9, a nucleic acid molecule according to any one of claims 14-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to claim 20 or claim 21, a compound according to any one of claims 22-24, or a pharmaceutical composition according to claim 31.

41. A method according to claim 40, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.

42. A method according to claim 41, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

43. A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to any one of claims 1-9, or the level of expression of a nucleic acid molecule according to any one of claims 14-17 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.

44. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 1-9, a nucleic acid molecule according to any one of claims 14-17, or a host cell according to claim 19 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.

45. A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to any one of claims 14-17; a second container containing primers useful

for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.

46. The kit of claim 45, further comprising a third container holding an agent for digesting unhybridised RNA.

47. A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to any one of claims 14-17.

48. A kit comprising one or more antibodies that bind to a polypeptide as recited in any one of claims 1-9; and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.

49. A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to any one of claims 1-9.

50. A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 49 with a candidate compound and determining the effect of the compound on the disease of the animal.